

DRUG POLICY

Sephience® (sepiapterin)

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the policy is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Sephience is indicated for the treatment of hyperphenylalaninemia (HPA) in adult and pediatric patients 1 month of age and older with sepiapterin-responsive phenylketonuria (PKU). Sephience is to be used in conjunction with a phenylalanine (Phe)-restricted diet.

POLICY

Required Documentation

Submission of the following information is necessary to initiate the prior authorization review:

1. Initial Requests:
 - a. Chart notes or medical records documenting past medical history of at least 2 blood phenylalanine measurements greater than or equal to 600 micromol/L
 - b. Chart notes or medical records documenting baseline phenylalanine level greater than or equal to 360 micromol/L prior to starting treatment with the requested medication
 - c. Chart notes or medical records documenting baseline renal function assessments (e.g., glomerular filtration rate [GFR])
 - d. Chart notes or medical records documentation and claims history of prerequisite therapy with a sapropterin product. If prerequisite therapies are not advisable, documentation of why therapies are not advisable for the member
 - e. Chart notes or medical records documenting member's current weight (within 60 days)
2. Continuation Requests:

- a. Chart notes or medical records demonstrating achievement or maintenance of a 30% decrease in phenylalanine levels from baseline, phenylalanine levels that are in an acceptable range (less than 360 micromol/L)
- b. Chart notes or medical records documenting member's current weight (within 60 days)

Prescriber Specialties

The requested medication must be prescribed by or in consultation with a physician who specializes in the treatment of metabolic disease and/or phenylketonuria (PKU).

Criteria for Initial Approval

Phenylketonuria (PKU)

Authorization of 3 months may be granted when all of the following criteria are met:

1. Member is one month of age or older
2. Member has been diagnosed with phenylketonuria and meets both of the following criteria:
 - a. Member has a clinical diagnosis of hyperphenylalaninemia (HPA) documented by past medical history of at least 2 blood phenylalanine measurements greater than or equal to 600 micromol/L
 - b. Member has a baseline phenylalanine level greater than or equal to 360 micromol/L prior to starting treatment with the requested medication
3. Member has not been diagnosed with hyperphenylalaninemia due to pathogenic variants in GCH1, PTS, QDPR, SPR, or PCBD1, consistent with a diagnosis of primary BH₄ deficiency
4. Member does not have any abnormal physical examination or laboratory findings indicative of signs or symptoms of renal disease including a calculated glomerular filtration rate (GFR) <60 mL/min/1.73 m²
5. Member has had an inadequate response, intolerance, or clinical reason to avoid a sapropterin product
6. Requested medication will be used in conjunction with a phenylalanine (Phe)-restricted diet
7. Requested medication will not be used in combination with sapropterin products or Palynziq (pegvaliase-pqpz)
8. Member's current weight is documented
9. Dose of the requested medication does not exceed 60 mg/kg/day

Continuation of Therapy

Phenylketonuria (PKU)

Authorization of 6 months may be granted when all of the following criteria are met:

1. Member meets one of the following criteria:
 - a. Achieved or maintained a 30% decrease in phenylalanine levels from baseline
 - b. Phenylalanine levels are in an acceptable range (less than 360 micromol/L)
2. Requested medication will be used in conjunction with a phenylalanine (Phe)-restricted diet
3. Requested medication will not be used in combination with sapropterin products or Palynziq (pegvaliase-pqpz)
4. Member's current weight is documented
5. Dose of the requested medication does not exceed 60 mg/kg/day

Other

Sepience (sepiapterin) is considered **not medically necessary** for members who do not meet the criteria set forth above.

Members currently receiving the requested medication as samples or via the manufacturer's patient assistance program will be required to meet the criteria for initial approval. This ensures that members are treated equally regardless of their provider's ability to access medication samples.

Dosing and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Non-Formulary Exception Criteria

Non-Formulary Exception criteria applies to formularies which do not include the requested product(s) on the formulary drug list. Meeting the criteria above may satisfy some, or all, portions of the Non-Formulary Exception Criteria. A medication that is non-formulary may be covered when the Criteria for Approval AND the following criteria are met:

1. The requested drug must be used for an FDA-approved indication, or an indication supported in the compendia of current literature (examples: AHFS, Micromedex, current accepted guidelines). Diagnostic testing/lab results required when applicable.
2. The prescribed dose/quantity must fall within the FDA-approved labeling or dosing guidelines found in the compendia of current literature.
3. All covered formulary alternative drugs on any tier will be ineffective, have been ineffective, would not be as effective as the non-formulary drug, or would have adverse effects. Documentation is required and must include chart note(s) or other documentation indicating prior treatment failure, severity of the adverse event (if any), and dosage and duration of the prior treatment, or contraindication to formulary alternatives.

Quantity Limits Apply

Medication	Standard Limit	FDA Recommended Dosing
Sephience (sepiapterin) 250 mg powder packet	3 powder packets per day	Sephience is administered orally once daily. Maximum daily dose is 60 mg/kg for all patients. Recommended starting dosage is based on patient's age: • <6 months: 7.5 mg/kg/day • 6 months to <1 year: 15 mg/kg/day • 1 year to <2 years: 30 mg/kg/day • 2 years and older: 60 mg/kg/day
Sephience (sepiapterin) 1000 mg powder packet	6 powder packets per day	Recommended titration in patients <2 years: • Check blood Phe level to determine response to treatment within 2 weeks • If blood Phe does not decrease, dosage may be titrated incrementally based on blood Phe levels to a maximum daily dosage of 60 mg/kg Discontinue in patients whose blood Phe does not decrease after 2 weeks of treatment at the maximum daily dosage of 60 mg/kg

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

REFERENCES

Sephience [package insert]. Warren, NJ: PTC Therapeutics, Inc.; July 2025.

Smith WE, Berry SA, Bloom K, et al. Phenylalanine hydroxylase deficiency diagnosis and management: A 2023 evidence-based clinical guideline of the American College of Medical Genetics and Genomics (ACMG). Genet Med. Published online December 2, 2024. doi:10.1016/j.gim.2024.101289

Singh RH, Rohr F, Frazier D, et al. Recommendations for the nutrition management of phenylalanine hydroxylase deficiency. Genet Med. 2014;16(2):121-131.

POLICY HISTORY

Policy #: 05.06.05

Original Effective Date: January 1, 2026

Reviewed: January 2026

Revised:

Current Effective Date: January 1, 2026